

## REMARKS

In the Disclosure, the paragraph starting on page 61, line 4 was amended to define the compound TH9507 by its structure.

Claims 1, 2 and 4 to 12 are now in the application.

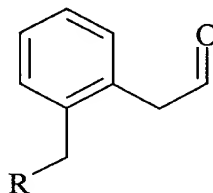
Claim 2 has amended to define the enantiomers and is supported at pages 11 and 12 of the original specification.

Claim 3 has been cancelled.

Claim 6 has been amended to correct the typographical error appearing in the term "drawfism".

Claim 12 has been added, and no new matter is added by new claim 12.

In complete response to the Requirement for Restriction mailed February 11, 2003, Applicants provisionally elect, albeit with traverse, to prosecute the claims of Group I, namely Claims 1 to 2 drawn to a compound, with the addition of the new claim 12 directed to a composition of matter comprising the compounds of claim 1, with the election of the following compound:



**R = H**

Reconsideration of the Restriction Requirement is however respectfully requested. The Examiner maintains in his Requirement for Restriction that the "special technical feature" relating the claims of Groups I-X, namely the compounds of claims 1 and 2 lack inventive step as shown by WO 96/37514.

The Applicant respectfully submits that WO 96/37514 teaches GRF analogs bearing a hydrophobic tail of C5 to C7 in length as having increased potency. However,

WO 96/37514 teaches away from the present invention in that it is not the length of the tail (C5 to C7) that contributes to the enhanced activity, but the rigidifying moiety in the chain as taught by the present invention (see pages 9 to 12).

The compounds claimed in claims 1 and 2 were not derived from testing a random library of "hydrophobic tails". The compounds were designed with the premise that a ring may have the same effect as a double bond in terms of increasing stability because it offers rigidity somewhat like a double bond. Indeed, analogs 1 to 7 (see pages 60, 61) synthesized and tested in the present application, are all more potent than natural GRF (see pages 61 to 63 and Day 6 in Figures 7A and 7B).

However, the degree of this enhanced potency is somehow linked to other features of the tail as can be seen by comparing the structures of analogs 1, 2 and 3 on page 60 (which are stereoisomers of the same structure) with their biological activity on Day 6 of Figure 7A. Indeed it shows that analog 1 which is a TRANS isomer is much less active than analogs 2 or 3 which are CIS isomers; in fact, it is hardly more active than GRF itself and less active than TH9507 where the rigidifying moiety is a double bond.

Another case in point is the comparison of analogs 6 and 7 on page 61 (which are positional isomers) with their biological activity on Day 6 of Figure 7B. Again, it shows, that while both compounds are very active with respect to natural GRF, the degree of enhanced activity varies greatly with the mere position of the methyl group on the benzene ring. In other words, the shape of the hydrophobic tail also seems to be of paramount importance. Furthermore, these two compounds bear 9 carbon atoms which is taught away by WO 96/37514.

For the reasons mentioned above, the compounds as claimed in claims 1 and 2 differ from, and represent an inventive step over, the compounds described in WO 96/37514. This inventive step, that the Examiner believed to be absent, is thus the special

technical feature which is common to the claims of Groups I to X forming therefore a single general inventive concept as required by PCT Rule 13.1.

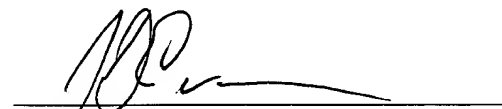
Therefore, it is respectfully submitted that these ten (10) groups (Group I to X) are closely connected together by a common special technical feature and that the search and examination of claims 1 to 12 of the application can be made without serious burden on the Examiner.

From the foregoing, the ten (10) groups of invention should therefore be rejoined and examination is solicited on claims 1 to 12 as pending.

In the event that there are any questions concerning this response, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #037116.49753US).

Respectfully submitted,



J.D. Evans  
Registration No. 26,269  
Christopher T. McWhinney  
Registration No. 42,875

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CROWELL & MORING, LLP  
P.O. Box 14300  
Washington, DC 20044-4300  
Telephone NO.: (202) 624-2500  
Facsimile No.: (202) 628-5116